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# Nutritional Supplements for Down Syndrome: A Highly Questionable Approach

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Down syndrome is a genetic disorder caused by the presence of a third 21st chromosome. It occurs once in every 600 to 700 births, making it the most common genetic disorder. Its common features include poor muscle tone, short stature, a small nose with flat nasal bridge, small skin folds on the inner corner of the eyes (epicanthal folds), dry skin, immune-system suppression, developmental delays, speech difficulties, and mental retardation.

Even before Down syndrome was found to be caused by a genetic abnormality, nutritional therapies were proposed, usually focusing on one or two items. Mixtures that included vitamins, hormones and enzymes were advocated in the 1960s by Haboud, a German physician [1]; however, other investigators found no beneficial effect [2]. At about the same time, Henry Turkel, MD, in the United States claimed that a mixture of 48 different ingredients could improve intelligence and the appearance of children with Down syndrome [3]. No double-blind study was ever performed with Turkel's **formula**. Dr. Turkel administered his **formula** to children with Down syndrome for almost 40 years; if there had been some benefit, we should have had such evidence by now. Yet no such group of children or adults have been identified to date.

In the 1980s, Ruth Harrell, MD, and associates [4] reported that supplementary vitamins and minerals and thyroid hormone improved their IQ scores, and caused "physical changes toward normal" among children with various types of mental deficiency, with the best results in three children with Down syndrome. However, the study was neither controlled nor blinded, and seven different studies during the next decade showed no positive results from Harrell's mixture. Haps Caps, another mixture of vitamins, minerals and enzymes that hit the marketplace during the 1980s, is frequently given with thyroid hormone. No study of Haps Caps has been published.

Harrell's **formula** gained notoriety because it was published in a scientific journal. Haps Caps is promoted through traveling clinics run by Jack Warner, M.D. of California. In recent years, two formulas have become even more popular because of TV shows, Internet promotion, and seminars. In 1995, ABC-TV's "Day One" promoted a **formula** created by Dixie Lawrence Tafoya, owner/operator of an adoption agency that specializes in finding homes for disabled children. Lawrence initially based her **formula** on Turkel's original mixture but modified it for her own daughter. The program described how Lawrence had adopted an girl with Down syndrome and had "tapped into medical databases, scoured libraries,

called research departments, talked to anyone who knew anything about the biochemistry of Down syndrome." The end result was a fomula based on Turkel's original mixture but containing many more ingredients. Subsequently, the drug piracetam was added to the child's regimen. During the program, her daughter's school principal and a special instruction teacher said the child had improved after taking the formula; whereas a National Down Syndrome Congress official said, "But until . . . it's proven that the potion is what made that improvement, we would be irresponsible to tell people to go get that."

By the time "Day One" aired, Lawrence's had arranged for her formula to be produced by Nutri-Chem Labs (a Canadian company) and the product was called MSB Plus, which differed considerably from previous formulas aimed at Down syndrome. In 1996, she withdrew her support from Nutri-Chem and began promoting a formula called NuTriVene-D, which is marketed by International Nutrition, Inc., of Baltimore, Maryland. Nutri-Chem still markets MSB Plus. Both formulas have more than 40 ingredients, most of them the same or similar, but with differences in dosage. Various formulas from other companies have not been as popular.

**Common Ingredients**

Down syndrome formulas contain four main groups of ingredients: vitamins, minerals, amino acids and anti-oxidants. Newer additions include digestive enzymes and fat supplements.

***Vitamins.*** Supplementation with both single vitamins and vitamin mixtures have been studied in children with Down syndrome. Although sporadic reports of vitamin deficiencies have been published [5,6], most studies reveal none [7-9], and many studies have found that vitamin supplementation with either RDA doses or megadoses have no effect on mental ability or behavior [10-19]. The present supplements tend to use RDA values, although levels of vitamin A high enough to be toxic are still occasionally promoted.

***Minerals.*** Several studies have shown zinc and selenium serum levels are decreased among children with Down syndrome. Some studies on zinc report increased growth, improved thyroid and lymphocyte functions, and increased survival of white blood cells with supplementation [21-28]; however, these are mostly unconfirmed [20,32]. Selenium is a cofactor in glutathione peroxidase, an enzyme that helps scavenge oxygen radicals. Selenium supplementation may improve certain indicators of immune functioning [29-31], but the supporting research has only been preliminary. There is no information on possible adverse effects of chronic zinc and selenium supplementation. No other mineral has been found either lacking or helpful in Down syndrome.

***Amino acids.*** All three popular formulas (MSB Plus, NuTriVene-D, and Haps Caps) include amino acids. This supplementation is based on a study of adults with Down syndrome published in 1992 by Jerome Lejeune, M.D. [33] This study reported a consistent deficiency of serine and excess of cysteine and lysine, which Lejeune felt were caused by overexpression of certain genes on the 21st chromosome. He postulated that the supplemental amino acids balanced the blood levels, making the biochemical workings of the body normal. However, a subsequent study of 22 children found no such abnormalities in serum or urinary amino acid levels [34]. Amino acid supplements can cause an unpleasant odor in the user's urine and sweat.

Some proponents claim that overexpression of the cystathione beta-synthase gene causes a "functional" folic acid deficiency in which serum levels are normal but the body can't use all of it and is unable to repair damaged DNA. Supplementation supposedly alleviates this alleged problem. This theory has yet to be demonstrated in a scientific study. The FDA has just funded such a study, which should be completed in 1999. However, it is not clear that cystathione beta-synthase levels are elevated in Down syndrome. One study showed increased amounts [35], but two others did not [36,37].

Another amino acid being promoted is tryptophan, which the body uses to synthesize serotonin. Decreased serum levels of serotonin have been found among people with Down syndrome [38]. However, it is not yet been possible to study serotonin levels in the brain, so it is not known whether the brain serotonin levels are also low. Oral administration of 5-hydroxytryptophan, a compound the body uses to make serotonin, has produced no apparent benefits [15, 38-40].

***Antioxidants.*** It has been known for many years that one of the genes overexpressed in Down syndrome is the one producing superoxide dismutase (SOD). This enzyme converts oxygen radicals, which are normal by-products of cell metabolism, to hydrogen peroxide and water. Glutathione peroxidase then converts the hydrogen peroxide to water and oxygen. One theory states that if there is more SOD without a corresponding increase in glutathione peroxidase, then more hydrogen peroxide will be available to cause peroxidative damage to the cell. Experiments with cell cultures and postmortem tests seem to show that this oxidative damage might cause premature aging, damage leading to senile dementia of the Alzheimer's type, and the early loss of brain cells seen in infants with Down syndrome [41,42]. The theory claims that antioxidant supplements may prevent and even reverse damage by peroxidation. However, no evidence of this oxidative damage has been found in living humans with Down syndrome, and the possibility of adverse effects from long-term use of large amounts of antioxidants has received little attention.

***Digestive enzymes.*** Parents are being told that their children with Down syndrome lack certain digestive enzymes, making it harder for them to get needed nutrients from the diet. There is no proof that people with Down syndrome are deficient in any pancreatic or intestinal enzyme. In fact, most children with Down syndrome have trouble with constipation, whereas people deficient in digestive enzymes tend to have loose stools. There does seem to be an increase in celiac disease in Down syndrome (a disorder of malabsorption), but enzymes do not help in this condition.

***Docosahexaenoic acid (DHA).*** This omega-3 fatty acid is an important constituent of cell membranes, especially in the retina and brain. Typically, DHA is synthesized in the body from other fatty acids in the diet. Studies have indicated that premature infants may not be able to synthesize enough on their own, so infant formulas for premature babies should be fortified with DHA. Because breast milk contains DHA, the World Health Organization and several other organizations have asked the FDA to include it in regular infant formulas in the US. (DHA is already a component in infant **formula** in several European countries.) Promoters of DHA for older children with Down syndrome claim that its use will improve eye and neurologic development. No research indicates that children with Down syndrome lack DHA, cannot make enough, or can benefit from DHA supplements. Further, studies have shown that the critical period for supplementing DHA in preterm infants is the first two months of life [43] and little benefit beyond that should be expected. Likewise, the promotion of the use of other fatty acids has no proven benefit for children with Down syndrome. The use of DHA entails some risks. Too much can actually suppress the immune system, which is already impaired in people with Down syndrome.

***Choline.*** Studies have shown that as children with Down syndrome age, there is a loss of neurons that produce the neurotransmitter acetylcholine. It is presumed that this loss may cause difficulties with memory and cognitive function. Choline is promoted for increasing myelinization of neurons and for increasing levels of the neurotransmitter acetylcholine. However, there is no evidence that oral choline supplements do either of these things in people with Down syndrome.

***Piracetam.*** Another product mentioned on the ABC show profiling Dixie Lawrence was piracetam. Piracetam was developed in the 1970s and has been studied as a possible treatment for several diseases, including Alzheimer's disease, sickle cell anemia, dyslexia and a movement disorder called myoclonus.

One study [44] seemed to show cognitive improvement in children with Down syndrome given piracetam, but the study was not blinded nor controlled by placebo. No other study on this topic has been published, though introductory studies are currently taking place. Piracetam has orphan drug status for myoclonus, but it is not FDA-approved for treating Down syndrome.

***DMSO (dimethyl sulfoxide).*** The Sierra Clinic, located in Mexico, is treating children with muscular injections of amino acids and DMSO in an attempt to improve cognition and motor skills. One study supports such use [45], but the study was not blinded and has not been confirmed by any other researcher. One study on oral DMSO in children with Down syndrome found no benefit [46].

**Adverse Effects**

When use of supplementary nutrients began, many of the vitamins were in megadose quantities. However, in response to criticism of the danger of toxicity, most regimens are now within RDA ranges. Vitamins A and E continue slightly above the RDA in several supplements. There is still concern as to infants who are nursing or taking **formula** and being given these products getting too much vitamin A and a heavy protein load. Information on side effects is not being collected systematically. However, at a meeting in late **1997** of the Down Syndrome Medical Interest Group, doctors caring for these children reported instances of diarrhea, hyperactivity, and insomnia. Another notable effect has been loss of appetite, related to the fact that these supplements are not usually palatable. Parents often hide them in food and drink. A few children have stopped eating, apparently suspicious that the supplement was in all their food. Orange skin coloring (carotenemia) was occasionally reported before vitamin A levels in these supplements were decreased.

**Questionable Promotions**

Supplement products have become a source of much debate and controversy in the Down syndrome community, largely because of the ways they are promoted. Here are some examples.

***Stating speculations as fact.*** Supplement promoters commonly claim that "infants with Down syndrome become retarded largely because of the overexpression of" superoxide dismutase, and that supplements can compensate for this. Some promoters append a long list of scientific articles to their promotional pieces, implying that they all support what the promoter has written. Generally, however, many of the studies have little to do with nutritional supplementation, and of those that do, the vast majority actually conclude that supplementation is not beneficial. Such lists can be very misleading to the parent with no medical background or a physician who lacks the time to investigate the actual articles or even read the abstracts..

***Dubious claims of benefits.*** The claims range from the mild, such as an increase in growth rate and decrease in rate of infections, to the extreme of normalizing such items as cognition, muscle tone, sleep habits, speech, visual acuity and even facial features. The Sierra Clinic even claims on its Web site that its treatment "turns the Down syndrome patient into a normal healthy individual."

***Targeted nutrition.*** The **NuTriVene-D** program is said to be specifically designed for individuals with Down syndrome -- to enable better absorption of nutrients and provide "essential nutrients that are typically deficient." [47] International Nutrition and the Trisomy 21 Research Institute refer to **NuTriVene-D** as "Targeted Nutrition Intervention" ("TNI"). However, they do not recommend testing vitamin and mineral levels before use of the product is begun (and do not recommend amino acid testing at all). No definitive research has been published showing consistent nutrient deficiencies among children with Down syndrome. When asked why the supplement is called "targeted" if no blood tests are done to

determine whether deficiency exists before it is used, proponents reply that the stock **formula** fits the needs of approximately 85% of all children with Down syndrome and that adjustments can be made later. **NuTriVene-D** is also promoted for use by children with other "chromosomal deletions or mutations, and other abnormalities." [48]

***Use of anecdotal evidence.*** Many parents report that their child improved after starting supplements. Stories of increased health, normal growth, children acting "brighter" or "more with it" are abundant and can be very alluring to the interested parent or doctor. However, such testimonials have been shown to be affected strongly by the parent's bias. Curiously, two studies in the 1980s using Harrell's **formula** showed that parents of the children taking the placebo were more likely to claim their child had shown improvement than were the parents of children taking the actual **formula** [16,19].

***Misrepresenting the nature of Down syndrome.*** Some promotional literature refers to Down syndrome as a "progressive, metabolic, degenerative disease that if left untreated, would lead to poor health, mental retardation and ultimately premature death." [49] Researchers and clinicians who have worked with adults with Down syndrome for years, if not decades, dispute this statement, as do current parents of adults with Down syndrome. The outlook for people with Down syndrome is not bleak, and each generation has had a healthier, longer lifespan. There is no evidence that any nutritional supplement enhances the prognosis. This tactic tends to prey mostly on the parents of infants and young children with Down syndrome, who are most vulnerable to the suggestion that they might be bad or neglectful parents if they don't give their children these products.

**The Bottom Line**

While a few vocal doctors have championed the idea that dietary supplements can help children with Down syndrome, most doctors who take care of these children on a day-to-day basis do not recommend supplements. In 1996, the American College of Medical Genetics stated that it knew of no scientific evidence that treatment with Piracetam or amino acid supplements can improve the mental functioning of people with Down syndrome [50]. In **1997**, the National Down Syndrome Society cautioned parents that:

> The administration of the vitamin related therapies -- e.g. the vitamin/mineral/amino acid/hormone/enzyme combination, has not been shown to be of benefit in a controlled trial, that the rationale **advanced** for these therapies is unproven, and that the previous use of these therapies has not produced any scientifically validated significant results. Moreover, the long term effects of chronic administration of many of the ingredients in these preparations are unknown. Despite the large sums of money which concerned parents have spent for such treatments in the hope that the conditions of their child with Down syndrome would be bettered, there is no evidence that any such benefit has been produced. [51]

Despite all this, however, the use of these supplements continue to be popular. An estimated 5,000 children with Down syndrome have been placed on one of these supplements.The number still taking them is unknown, but interest in these treatments remains high. Told that the nutritional therapies can't hurt and might help, many parents decide that the therapies are "worth a try." Also, with so much research in Down syndrome focusing on prenatal testing or presenile dementia, many parents feel abandoned by the medical establishment. For these parents, the supplement promoters seem to be the only ones interested in "ending the implications of Down syndrome," as one newsletter puts it.

No matter how alluring the theories are, or how convincing the anecdotal evidence may seem, it's important to remember that these theories have not been proven, past experience with similar claims have been proven unhelpful, and the currently promoted formulas have not been scientifically proven safe or

effective.

## About the Author

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